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## Editorial

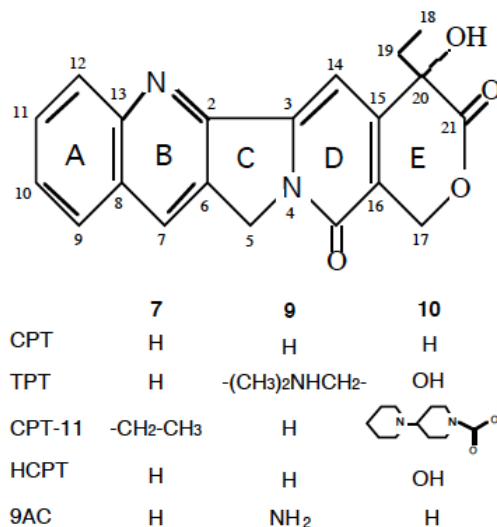
Development of *Camptotheca* Decaisne as Pharmaceutical Crops

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*Camptotheca* Decaisne is a genus of the family Nys-saceae native to China. It is the major natural source of camptothecins (CPTs), anti-cancer alkaloids. CPTs (Fig. 1) have shown promising anti-cancer activity in almost all kinds of cancer in clinical trials in the USA, China, Japan, and Europe since 1957, and especially those since 1986 [1]. The CPT agents have also shown potent anti-viral activity against HIV in both animal and human cell cultures [2]. In 1996, Topotecan (TPT, Hycamtin®) and Irinotecan (CPT-11, Camptosar®), two semi-synthetic CPT drugs were approved by the FDA for the treatment of patients with advanced ovarian and colon cancer, respectively. In 1998, Topotecan was approved by the FDA for treatment of small cell lung cancer. 9-Nitrocamptothecin (9-NC, Rubitecan), 9-Aminocamptothecin (9-AC) and several other CPT analogs (e.g., CZ112) also show promising results in clinical trials. In fact, CPT agents have been recognized as the most promising anti-cancer drugs in the world. Therefore, worldwide demand for CPTs is dramatically increasing. Currently, CPT production is still dependent on natural supply. However, *Camptotheca* trees grow rapidly, and many parts of the tree can be used to extract drug CPTs.

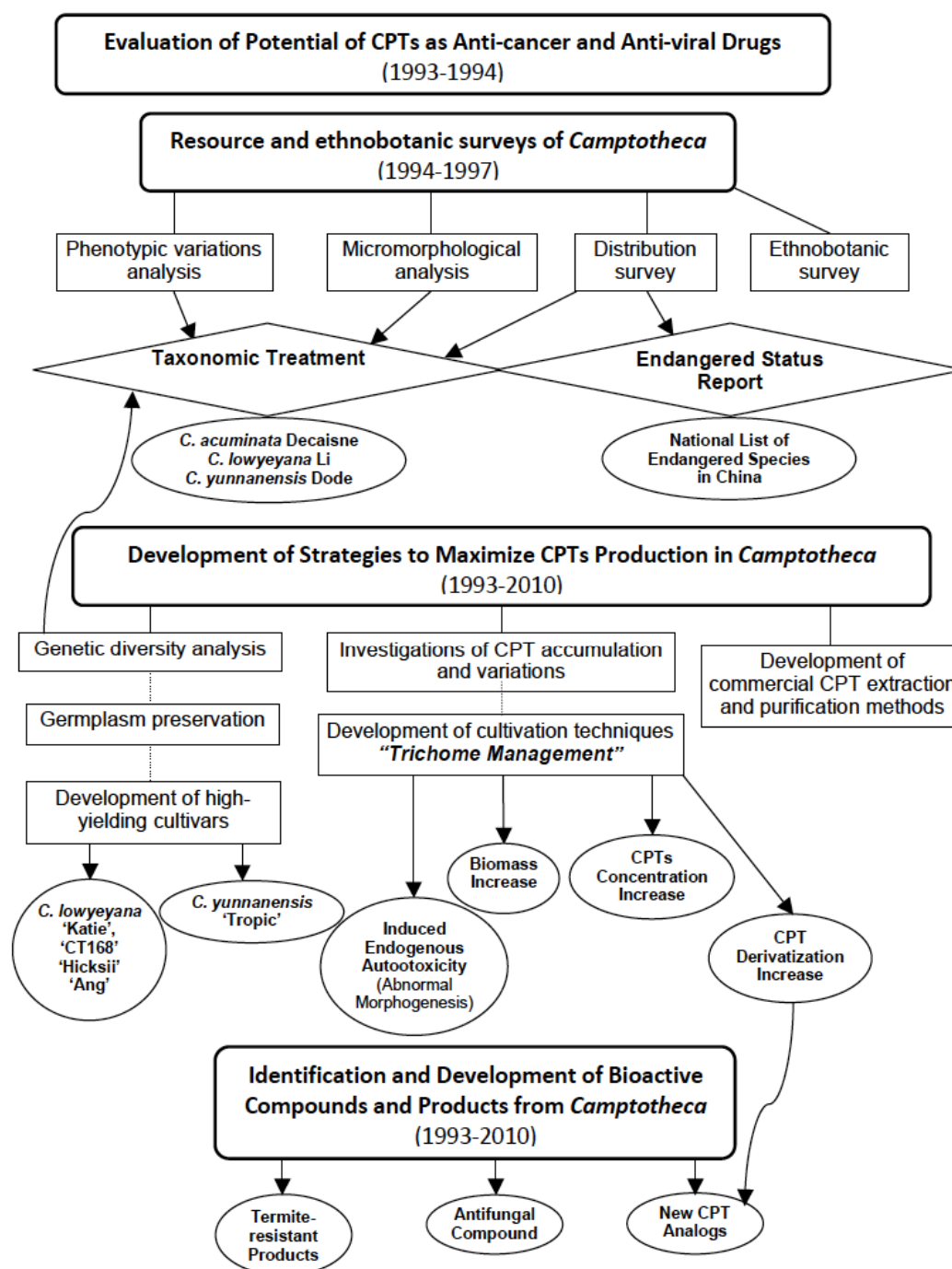
The earliest record of the *Camptotheca* tree dated back to 1848 in the Chinese book, *Zhi Wu Ming Shi Tu Kao* [1]. Until 1965, when CPT was first isolated from *Camptotheca* [3], only 25 publications were available worldwide on *Camptotheca*; and all of these to treating only botanical aspects [1]. By February 2000, 540 patents had been granted worldwide and approximately 1,500 journal articles had been published. Over 95% of the publications, however, dealt with either chemical or medical aspects of CPTs with only about 5% focusing on the *Camptotheca* tree, itself. Principal research studies on *Camptotheca* taxonomy [4-6], anatomy and morphology [1, 7-10], phylogeny [11-13], embryology [14], chromosome numbers [15], pollination biology [14, 16, 17], geography [1, 18, 19], and physiology [20-22].



**Fig. (1).** Chemical structure of camptothecin (CPT) and its main derivatives as anti-cancer drugs in clinical treatments and trials.

Obviously, a systematic study of *Camptotheca* as pharmaceutical crops for production of CPTs is needed. Theoretically, taxonomic and genetic diversity, and CPT production ecology are still poorly understood. Our studies have identified at least three problems with the development of *Camptotheca* as a source for CPTs. First, *Camptotheca* is an endangered genus whose wild populations may possibly be nearing extinction. Second, the gene pool of *Camptotheca* in the USA is extremely small. Most of the trees in the USA are traceable to only two mature trees in Chico, California, that germinated from seeds imported from southern China in 1934. Selfing is often the only natural breeding system for the *Camptotheca* trees in USA; and these offsprings are normally of low quality. In addition, asexual propagation is the method commonly used to reproduce *Camptotheca* seedlings in the USA. Third, cold-hardiness and drought-tolerance are two major problems in the development of plantations in the southeastern USA. The present genetic resource base of *Camptotheca* in the USA is too small to select for either cold-hardiness, drought-tolerance, or high-CPT-yielding genotypes.

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**Fig. (2).** Strategies to develop *Camptotheca* as pharmaceutical crops at the National Center for Pharmaceutical Crops, Arthur Temple College of Forestry and Agriculture, Stephen F. Austin State University, Nacogdoches, Texas, USA.

To solve the above problems, researchers at National Center for Pharmaceutical Crops, Arthur Temple College of Forestry and Agriculture, Stephen F. Austin State University began our *Camptotheca* research project in the early 1990s. The financial support has been received from the Houston Livestock Show and Rodeo, the Fondren Foundation, Stephen F. Austin State University, Chinese Ministry of Forestry, David Dolben, Jack Hicks, and Charles Poland. To develop *Camptotheca* as pharmaceutical crops, the studies have been conducted in four aspects from 1993 to 2010 (Fig. 2):

1. Evaluation of the potential of CPTs as anti-cancer and anti-viral drugs [1] (1993-1994).
2. Investigation of the *Camptotheca* resource worldwide, including distribution (identification of its endangered status), phenotypic variations, micromorphological analysis, taxonomic treatment (the discovery and description of new species) [6], and ethnobotanical survey (1994-1997).
3. Development of strategies to maximize CPTs production in *Camptotheca*, including the establishment of an exclu-

sive germplasm preserve, the detection of genetic diversity with DNA RAPD markers, the development of a high-CPT-yielding cultivar [23], the discovery of CPT accumulation sites in trees [24], strategy development for induced production of CPT in plants [25], discovery of induced endogenous autotoxicity (abnormal morphogenesis) following decapitation pruning [26], and the improvement of CPT extraction methods (1993-2010).

4. Identification of new bioactive compounds and products, including isolation of new anti-tumor CPT analogs [27], identification of new antifungal compounds [28, 29], development of termite control products [30] (1997-2010).

This special issue primarily includes unpublished research data in taxonomy, phenotypic and micromorphological variations, anatomy, genetic variations, distribution, ethnobotany, cultivar development, and trichome management and overview of chemical composition at National Center for Pharmaceutical Crops, Arthur Temple College of Forestry and Agriculture, Stephen F. Austin State University. These articles may provide useful data fundamental to the conservation of the species as well as various strategies to develop and manage *Camptotheca* as pharmaceutical crops. This special issue will also include research report on other plant sources of CPTs at the University of Puerto Rico.

## CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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Specimen examined for plant taxonomy are deposited in the following herbaria: A, ASTC, BM, C, CDBI, E, HNU, IBSC, K, KUN, MO, O, P, PE, SZ, US, and WUK. Voucher specimen used for chemical analysis are deposited in the National Center for Pharmaceutical Crops, Arthur Temple College of Forestry and Agriculture, Stephen F. Austin State University.

## PATIENT'S CONSENT

Declared none.

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